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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/584,618 | 06/26/2006 | Hiroyuki Kamiya | 2006_1028A | 9673 |

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| EXAMINER | |
|---|---|
| MINNIFIELD, NITA M | |
| ART UNIT | PAPER NUMBER |
| 1645 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/584,618 | KAMIYA ET AL. | |
| | Examiner | Art Unit | |
| | N. M. Minnifield | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *12-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Applicants' amendment filed June 29, 2009 is acknowledged and has been entered. Claims 1-19 are pending in the instant application. All rejections have been withdrawn in view of Applicants' comments with the exception of those discussed below.

2. Claims 12-19 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 5, 2008.

3. Claims 1-11 have been examined in the instant application.

4. Receipt is acknowledged of papers (PCT/JP2004/017647 filed 11/19/04 and JP2003-431007 filed 12/25/03) submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The claimed invention gets priority to December 25, 2003.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite in the recitation of "derivative thereof", the metes and bounds of this phrase has not been defined. Claims 1, 6, 7, 10 and 11 are vague and indefinite in the recitation of "special nucleic acid base", what are the metes and bounds of the term "special"?

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 1, 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Brunner et al (J. Immunology, 2000, 165:6278-6286).

Brunner et al discloses CpG containing oligonucleotides, which mimic the immunostimulatory effect of bacterial DNA (abstract). Brunner et al discloses that these oligonucleotides induce cytokine production (abstract). Brunner et al discloses that synthetic oligodeoxynucleotides containing unmethylated cytidine-phosphate-guanosine (CpG) dinucleotides (CpG-ODN) in specific sequence contexts mimic the immunostimulatory qualities of bacterial DNA. In vitro, they up-regulate the expression of costimulatory and Ag-presenting molecules and the secretion of IL-12 by monocytes and DC. In vivo, CpG-ODN act as an adjuvant, promoting Th1 immune responses that can enhance promotion from a subsequent tumor challenge when coadministered with tumor Ag." (p. 6278, right column) Brunner et al discloses in vitro methods of producing an inflammatory cytokine (i.e. TNF-$\alpha$, IL-12) using cultured cells (materials and methods). The prior art anticipates the claimed invention.

The rejection is maintained for the reasons of record. Applicants' arguments filed June 29, 2009 have been considered, but they have not been deemed persuasive. It is noted the claims do not define the source of the nucleic acids. The abstract states that the synthetic nucleic acids

mimic bacterial DNA not that they are bacterial DNA. The claims do not recite that the nucleic acid base can't exist naturally. With regard to Applicants' analysis of claim 6 in the arguments concerning the Brunner et al rejection, the Examiner points out that claim 6 is not a part of this rejection.

10. Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Karras (6727064, filing date January 11, 2001).

Karras discloses a nucleic acid containing a special nucleic acid base or derivative thereof (see description, para. 34, 49, 51). It is noted that an oligonucleotide analog is a derivative thereof. Karras discloses that the modified nucleobase (i.e. special nucleic acid base). "Oligonucleotides may also include nucleobase (often referred to in the art simply as "base" or ("hetero-cyclic base moiety") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases also referred herein as heterocyclic base moieties include other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine." (description, para. 51)

It is noted that the specification broadly describes a derivative thereof: "In the invention of this application, the derivative of the nucleic acid containing the special nucleic acid base may be used. This "derivative" is a substance whose phosphoric acid moiety or sugar moiety is modified in using a chemical synthetic product, a substance with a structure other than a base moiety changed or the like." (p. 12, l. 1-7) The prior art anticipates the claimed invention.

It is noted that the recitation of "immunopotentiator" in the preamble of the claim is viewed as intended use, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Since the Patent Office does not have the facilities for examining and comparing applicants' products with the products of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed products and the products of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 1-4 and 6-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Raz et al (US 2002/0042387, publication date February 22, 2001).

Raz et al discloses Applicants' claimed SEQ ID NO: 2 (see Raz et al, SEQ ID NO: 7) as well as modified nucleic acid bases (see below, claims). "[0034] The terms "oligonucleotide," "polynucleotide," "sequence," and "nucleic acid molecule", used interchangeably herein, refer to polymeric forms of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. Thus, this term includes, but is not limited to, single-, double-, or multi-stranded DNA or RNA, genomic bacterial DNA, plasmid DNA, CDNA, DNA-RNA hybrids, or a polymer comprising purine and pyrimidine bases or other natural, chemically or biochemically modified, non-natural, or derivatized nucleotide bases. The backbone of the polynucleotide can comprise sugars and phosphate groups (as may typically be found in RNA or DNA), or modified or substituted sugar or phosphate groups. Alternatively, the backbone of the polynucleotide can comprise a polymer of synthetic subunits such as phosphoramidites, and/or phosphorothioates, and thus can be an oligodeoxynucleoside phosphoramidate or a mixed phosphoramidate-phosphodiester oligomer."

"[0048] The phosphorous derivative (or modified phosphate group) that can be attached to the sugar or sugar analog moiety in the modified oligonucleotides of the present invention can be a monophosphate, diphosphate, triphosphate, alkylphosphate, alkanephosphate, phosphorothioate, phosphorodithioate or the like. The heterocyclic bases, or nucleic acid bases that are incorporated in the oligonucleotide base of the ISS can be the naturally occurring principal purine and pyrimidine bases, (namely uracil or thymine, cytosine, adenine and guanine, as mentioned above), as well as naturally occurring and synthetic modifications of said principal bases. Those skilled in the art will recognize that a large number of "synthetic" non-natural nucleosides comprising various heterocyclic bases and various sugar moieties (and sugar analogs) are available, and that the immunomodulatory nucleic acid molecule can include one or several heterocyclic bases other than the principal five base components of naturally occurring nucleic acids. Preferably, however, the heterocyclic base in the ISS is selected from uracil-5-yl, cytosin-5-yl, adenin-7-yl, adenin-8-yl, guanin-7-yl, guanin-8-yl, 4-aminopyrrolo [2,3-d] pyrimidin-5-yl, 2-amino-4-oxopyrolo [2,3-d] pyrimidin-5-yl, 2-amino-4-oxopyrrolo [2,3-d] pyrimidin-3-yl groups, where the purines are attached to the sugar moiety of the oligonucleotides via the 9-position, the pyrimidines via the 1-position, the pyrrolopyrimidines via the 7-position and the pyrazolopyrimidines via the 1-position." "[0049] Structurally, the root oligonucleotide of the immunomodulatory nucleic acid molecule is a non-coding sequence that can include at least one unmethylated CpG motif. The relative position of any CpG sequence in ISS with immunomodulatory activity in certain mammalian species (e.g., rodents) is 5'-CG-3' (i.e., the C is in the 5' position with respect to the G in the 3' position)."

It is noted that the recitation of "immunopotentiator" in the preamble of the claim is viewed as intended use, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*,

535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Since the Patent Office does not have the facilities for examining and comparing applicants' products with the products of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed products and the products of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

12. Claims 1-3 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Moriya (PNAS USA, February 1993, 90:1122-1126).

Moriya discloses a vector (i.e. plasmid) having modified nucleic acid bases (abstract, title). Moriya discloses 8-Oxoguanine. The plasmids disclosed include pMS2, pMS2(dG), pMS2(8-oxodG) (see materials and methods). The prior art also discloses nucleic acid containing non-methylated CpG sequences (see also Tables and figures).

It is noted that the recitation of "immunopotentiator" in the preamble of the claim is viewed as intended use, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Since the Patent Office does not have the facilities for examining and comparing applicants' products with the products of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed products and the products of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

13. Claim 2 is objected to because of the following informalities: Please see line 5 of the claim. Does Applicant intend "dimmer" or is it "dimer"? Appropriate correction is required.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/
Primary Examiner, Art Unit 1645
November 20, 2009